CiRA Generates Safer induced Pluripotent Stem (iPS) Cells

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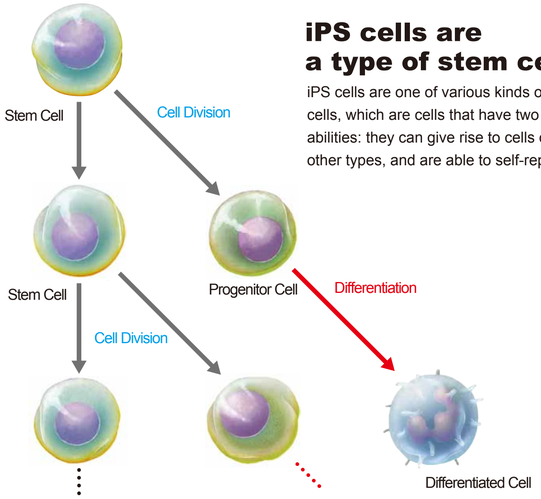
1 What are iPS Cells?

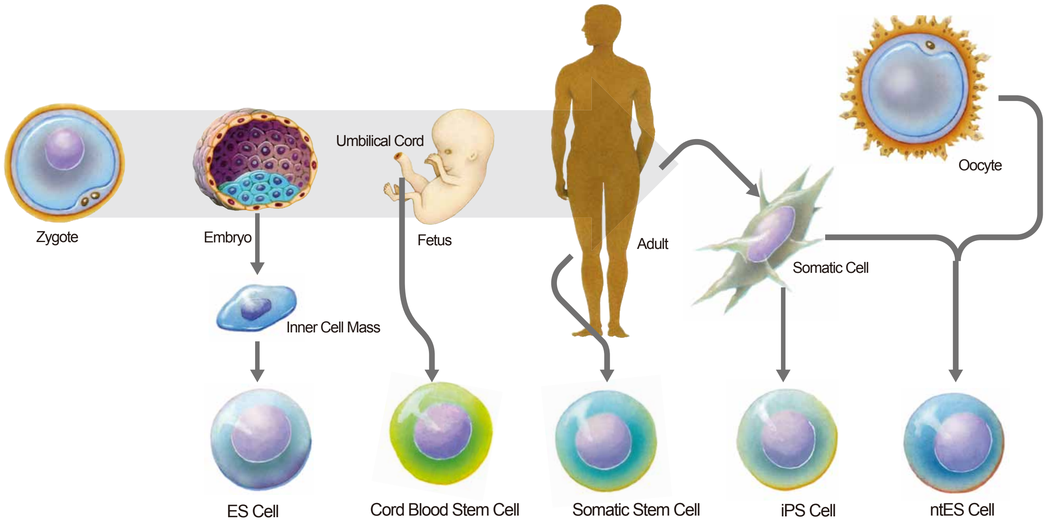


iPS cells are a type of stem cells

iPS cells are one of various kinds of stem cells, which are cells that have two important abilities: they can give rise to cells of other types, and are able to self-replicate.

Induced pluripotent stem cells

There are stem cells, called “adult” or “somatic” stem cells, in all of our bodies, which can be found in specific kinds of tissues and locations, and which give rise to specific types of cells. These stem cells give rise to other cells in response to signals from their environments. In addition to these naturally occurring stem cells, there are other types that can be generated artificially, or “induced.” These include embryonic stem (ES) cells and induced pluripotent stem (iPS) cells. ES and iPS cells differ from somatic stem cells in that they can give rise to all types of cells. This capability is known as “pluripotency,” and ES and iPS cells are collectively referred to as pluripotent stem cells.

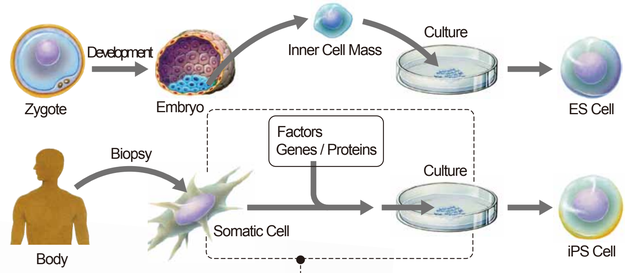


	ES Cell	Cord Blood Stem Cell	Somatic Stem Cell	iPS Cell	ntES Cell
Origin	Embryo	Cord Blood	Tissue	Somatic Cell	Somatic Cell & Oocyte
Pluripotency	○	×	×	○	○

ES Cells ES (Embryonic stem) cells are a kind of pluripotent stem cells produced by culturing cells collected from blastocysts on day 3.5 after fertilization. ES cells can give rise to any of the many different cell types in the body.

ntES Cells Stem cells derived from somatic cells are called ntES cells (nuclear transfer embryonic stem cells), i.e., ES cells created from somatic cell-cloned embryos prepared using a nuclear transfer technique. ntES cells containing the same genetic information as that of the somatic cell donor can be created because the genetic information is derived from the donor cells.

2 iPS Cells are Born!

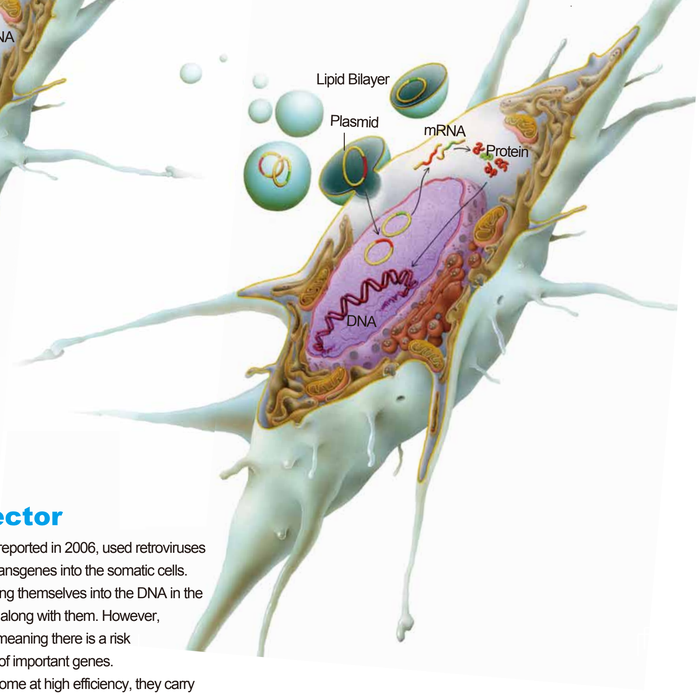


How are iPS and ES cells different?

The biological sources of ES and iPS cells are different. ES cells are derived from early embryos, a few stages after fertilization. ES cells are cells that have been removed from an embryo and grown in culture. In contrast, iPS cells are generated from somatic cells. They can be made by introducing a set of factors, such as the genes (Oct3/4, Sox2, Klf4, c-Myc) used in the first generation of iPS cells, into somatic cells, such as skin cells. After a few weeks of culture, some of these somatic cells are reprogrammed to a state of pluripotency, and iPS cells are born.

Retro Viral Vector

The first generation of iPS cells, reported in 2006, used retroviruses as “vectors” for introducing the transgenes into the somatic cells. Retroviral vectors work by inserting themselves into the DNA in the nucleus, and carrying the genes along with them. However, they insert at random locations, meaning there is a risk that they will disturb the function of important genes. So, while they insert into the genome at high efficiency, they carry this risk of causing unpredictable mutations and potentially even triggering tumor growth.



Plasmid Method

Plasmids are small circular DNA of bacterial or yeast that remain independent from the chromosomes. iPS cells have also been created using plasmids which encode the four transgenes. This plasmid method has the potential advantage of being able to introduce foreign genes without the risk of genomic mutations or tumors.

illustrations by Tomo Narashima

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